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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/245,615	02/04/1999	JAMES P. HOEFFLER	IVGN 274.1	5087

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INVITROGEN CORPORATION
C/O INTELLEVATE
P.O. BOX 52050
MINNEAPOLIS, MN 55402

EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

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06/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/245,615	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2006 and 26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-37,39,40,51,52,54-56,58-76 and 79-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-37, 39-40, 51-52, 54-56, 58-76, 79-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants' response to the non-final office action mailed 08 August 2006 is acknowledged (Paper filed 12/8/06). In the amendment filed therein claims 32, 74, 75, 76 and 79 were modified. New claims 81-83 were added. Currently claims 31-37, 39-40, 51-52, 54-56, 58-76 and 79-83 are pending and under consideration.

2. Rejections and/or Objections of record not reiterated below have been withdrawn.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

4. The information disclosure statements filed 9/8/06 has been considered as to the merits before Final Action.

REJECTIONS WITHDRAWN

Sequence Non-Compliance

5. This application has been updated to meet the sequence compliance requirements. In particular, the specification includes SEQ ID NO:1 on page 24, line 22 for Phe-His-His-Thr-Thr. The CRF has been submitted and entered. Accordingly the rejection is withdrawn.

NEW GROUNDS OF REJECTIONS

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 76 and 79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to microarray/kit configurations comprising specific antibody embodiments of 1000 different antibodies. However, support for the specific claimed embodiments is not found in the disclosure. Accordingly, the limitations are deemed new matter.

Response to Arguments

Applicant contends that the specification supports the recited 1000 different antibodies on page 3 lines 12-14. Specifically, the disclosure states: "Recently new technologies have arisen that allow the creation of microarrays containing thousands or millions of different elements." This was carefully considered but not found persuasive because the different elements were never taught to be different antibodies.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 70-73and 80 are rejected under 35 U.S.C. 102(b) as being anticipated by Shalon et al. (WO 95/35505).

Shalon et al. teach microarrays with immobilized reagents. The immobilized reagents include antibodies and antibody fragments that are dispensed on selected array positions. See abstract, page 11 lines 15-24, and page 31 lines 32-35, for example.

The discrete positions on the microarray are spaced apart (spatially addressable) on the solid support. See page 5 line 33, page 6 line 2, page 7 line 26-27. The source (cell line or cell type) of the antibodies at each discrete location is known (claim 55). See page 12 line 32 through page 13 line 2.

In one embodiment the microarray is treated to reduce non-specific binding with a polycationic polymer. See page 7 lines 30-32. The microarray has reagents (antibodies) spotted in discrete positions between 0.01 nanoliters and 100 nanoliters. See page 6 lines 8-10. The microarray also comprises regions from 100 locations per square centimeter to 1000 locations per square centimeter (reading on claim 64 and 73). Page 12 lines 3-9.

Response to Arguments

With respect to claims 70-73 and 80, the reference to Shalon et al. was reconsidered and deemed prior art under 35 USC 102. Accordingly the new rejection has been applied above.

With respect to claims 70-73, Applicant argues that neither Shalon et al. nor Schuh et al. teach antibodies that recognize proteins of a first species. This argument was carefully considered but not found persuasive because both Shalon et al. and Schuh et al. disclose antibody arrays having utility in antigen binding procedures (recognizing proteins of a first species). See Shalon et al. page 2 lines 8-10, pages 11-12, and page 31 lines 32-35, for example. See Schuh et al. page 61, second column 2nd paragraph, for example. Further, antibodies necessarily bind antigens/proteins.

Applicant contends that Schuh exemplifies several antibodies including "rat monoclonal antibodies that recognize human proteins" or proteins of a first mammalian species. See page 11, 2nd paragraph of Applicant's response filed 12/8/06. This argument was carefully considered but not found persuasive because "rat monoclonal antibodies that recognize human proteins" reads on the instant claims which broadly recite any antibody that recognizes or binds any protein of any species/mammalian. Also, a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 37, 55, 56, 58, 59, 63, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67).

Please see Shalon et al. as set forth above.

Shalon et al. differ from the instant invention in not specifically teaching that the antigen specificity of the antibodies is unknown.

However, Schuh et al. disclose ELISA-microtiter procedures involving the identification of monoclonal antibody specificity (antigen binding) at an early stage. See abstract. The antibodies are absorbed to microtiter wells and incubated with a labeled antigen preparation (such as a biotinylated cell lystate). See page 61 1st column. In one embodiment, two results are compared to identify the different cell lystates employed. See page 63 2nd column. The method was utilized to characterize monoclonal antibodies against both soluble proteins from mouse CIq, human CIq (antibodies recognizing proteins of a first species), and membrane determinants (like human pan T cells CD5 and CD7).

The major advantages of the screening technique are (i) the use of non-radioactive label resulting in an easy and time-saving procedure, (ii) the possibility of quantitating the amount of captured and detached antigen by ELISA, (iii) the procedure requires only a minimal amount of antigen, (iv) the procedure can be used with unpurified antibodies of all isotypes, (v) a high signal to noise ratio, and (vi) the possibility of detecting SDS-sensitive epitopes and of using crude antigen preparations. The identification of antibody specificity can be rapidly conducted at the early stages of hybridoma production. See abstract. The early identification of antibody specificity is taught to be very valuable. See page 65 2nd column.

Shalon et al. disclose antibodies immobilized on microarrays while Schuh et al. teach the utility of wherein the antigen specificity is unknown with labeled cell lysates. With respect to claim 80, it is noted that Schuh et al. disclose a reagent (peroxidase (HRP)-labeled avidin) for labeling a biotinylated cell lysate on page 61 1st column.

It would have been obvious to one of ordinary skill in the art to employ antibodies with unknown antigen specificity as taught by Schuh et al. in the microarray of Shalon et al. because Schuh et al. taught that the identification of antibody specificity can be rapidly conducted at the early stages of hybridoma production. See abstract. The early identification of antibody specificity is taught to be very valuable. See page 65 2nd column.

Further, this procedure had several advantages, including (i) the use of non-radioactive label resulting in an easy and time-saving procedure, (ii) the possibility of quantitating the amount of captured and detached antigen by ELISA, (iii) the procedure requires only a minimal amount of antigen, (iv) the procedure can be used with unpurified antibodies of all isotypes, (v) a high signal to noise ratio, and (vi) the possibility of detecting SDS-sensitive epitopes and of using crude antigen preparations. See abstract.

One of ordinary skill in the art would have been motivated to test antibodies of unknown antigen specificity in order to rapidly and simply identify antibody specificity at an early stage. See Schuh et al. page 59-60 – Introduction.

Response to Arguments

Applicant contends that Schuh exemplifies several antibodies including "rat monoclonal antibodies that recognize human proteins" or proteins of a first mammalian species. See page 11, 2nd paragraph of Applicant's response filed 12/8/06. This argument was carefully considered but not found persuasive because "rat monoclonal antibodies that recognize human proteins" reads on the instant claims which broadly recite any antibody that recognizes or binds any protein of any species/mammalian.

Also, a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Schuh et al. taught that the identification of antibody specificity can be rapidly conducted at the early stages of hybridoma production. See abstract. The early identification of antibody specificity is taught to be very valuable. See page 65 2nd column.

With respect to claims 37, 55, 56, 58, 59, 63 and 64, Applicant contends that there is no teaching in Shalon et al. that a bound antigen could be eluted from an antibody microarray in quantities that could be detected on a gel or blotted membrane as disclosed in Schuh. Therefore the combination of Schuh which detects Western blot elution of the antigen can not be combined with the binding array of Shalon et al.

This argument was carefully considered but not found persuasive because Schuh et al. are not limited to Western blot elution measurements of the antigen but also disclose that the combination of microtiter plates and biotin labeling can be utilized to quantify the amount of bound antigen according to standard ELISA procedures .....without the need for carrying out the whole electrophoretic and binding procedure. See page 66 1st column - 3rd paragraph.

The test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See In re Bent, 52 CCPA 850, 144 USPQ 28 (1964); In re Nievelt, 179 USPQ 224 (CCPA 1973).

Accordingly the rejection is maintained.

Response to Applicant's Arguments against Examiner's Prior Arguments

Arguments presented on pages 17 and 18 of paper filed 12/8/06.

Applicant contends that Shalon et al. in view of Schuh et al. do not provide a reasonable expectation of success with respect to the *use* of the arrays of Shalon et al. in the method of Schuh et al. because the method of Schuh et al. requires more antigen than a skilled artisan would expect to present on a microarray. This argument was carefully considered but not found persuasive because the instant claims are drawn to microarray or kits comprising microarrays not to methods of use. A "use" can only be properly claimed as a process or method. 35 USC 100(b), 101. See, Clinical Products v. Brenner, 255 F. Supp. 131, 149 USPQ 475, 477 (DDC 1966). In re Thuau, 1943 CD 390. Further, the utility of the microarray taught by the combination of Shalon et al. in view of Schuh et al. is not limited to the methods set forth in Shalon et al. in view of Schuh et al. In this case, the microarrays are taught to be useful in antibody screening (See Shalon et al. abstract, page 11 lines 15-24, and page 31 lines 32-35, for example and Schuh et al. page 59-60 – Introduction, for example) and is irrespective of the amount of antigen required because the claims do not specify an antigen amount.

Applicant argues that microarray and ELISA plate procedures are incompatible and would therefore render the methods unsatisfactory for its intended purpose. First the instant methods are not directed to methods. Secondly, microarray and ELISA applications have been taught to be compatible by the prior art. Evidence of this is found in the abstract to Seurynck-Servoss et al. wherein ELISA (microarrays) are one in the same. Accordingly the argument wasnot found persuasive.

III. Claims 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) as applied to claims 37, 55, 56, 58, 59, 63, 64, 70-73, and 80 above, and further in view of Ragg and Whitlow (FASEB, Vol.9, January 1995, pages 73-80).

Please see previous discussion of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) as set forth above.

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) differ from the instant invention in not teaching antibody fragments such as single chain/stranded recombinant antibody compositions.

However, Raag and Whitlow disclose single chain recombinant antibody fragments (sFv) consisting of only the variable light chain (VL) and variable heavy chain (VH) domains covalently linked by a polypeptide linker. Because the single chain recombinant antibody fragments are small they have rapid pharmacokinetics and tumor penetration in vivo. See abstract.

These single chain recombinant antibody fragments are derived from the antigen-binding domain of antibodies and are useful in any molecular recognition or binding application. See page 74 2nd column 2nd paragraph. SFv's are disclosed as tine reducers in ELISA applications. See page 74 2nd column middle of the 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibody fragments like recombinant single chain/stranded antibodies (sFv) as taught by Raag and Whitlow in the microarray of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) to produce arrays to perform multiple sample analysis in the rapid detection systems because Raag and Whitlow taught that sFv's were small allowing for rapid penetration (abstract), useful in any antibody application (page 74 2nd column 2nd paragraph), and reduced time in ELISA procedures page 74 2nd column middle of the 3rd paragraph.

Response to Arguments

Applicant argues that Ragg and Whitlow do not make up for the deficiencies of Shalon et al. and Schuh et al. This argument was carefully considered but not found persuasive because the combination of Shalon and Schuh has been addressed a priori and was maintained. Accordingly the instant rejection is maintained.

IV. Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Kohler et al. (Nature, 256, August 7, 1975, pages 495-497).

Please see previous discussion of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) as set forth above.

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) differ from the instant invention in not teaching that the source of the antibodies is from a known hybridoma cell line.

However, Kohler et al. teach antibody production from a known hybridoma cell (tissue culture cell lines made from fused myeloma and spleen cells from an immunized donor). Kohler et al. disclose that the production of antibodies via hybridoma is a satisfactory source of monoclonal antibodies of predefined specificity.

The cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph. The specification teaches that the reference of Kohler et al. teaches hybridoma procedures on page 8 lines 13-19.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize hybridoma cells to produce antibodies as taught by Kohler et al. in the antibody microarray of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) because Kohler et al. taught that hybridoma cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph.

Response to Arguments

Applicant argues that Kohler does not make up for the deficiencies of Shalon et al. and Schuh et al. This argument was carefully considered but not found persuasive because the combination of Shalon and Schuh has been addressed a priori and was maintained. Accordingly the instant rejection is maintained.

With respect to claim 79, it is noted that priority to 2/4/98 has not been granted because support for the claims has not been exemplified in the originally filed application. Accordingly the claims have been given a priority date of 5/17/06 (the date the claims were filed) for prior art rejections. Applicant is invited to show support for claim 79.

V. Claim 79 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) as applied to claims 37, 55, 56, 58, 59, 63, 64, 70-73, and 80 above, and further in view of Dolores J. Cahill (Journal of Immunological Methods, 250, 2001m pages 81-91).

Please see previous discussion of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) as set forth above.

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) differ from the instant invention in not teaching the utility of a plurality/collection of antibody 1000 different antibodies.

Cahill teach protein and antibody arrays and their utility in medical applications. See abstract. Antibody arrays are disclosed to be useful in the detection of proteins, the level of expression of proteins, and the correlation of protein expression in normal versus tumor (disease) tissue. See page 81 2nd column. Antibody arrays provide high throughput approaches, which allow for the generation and arraying of thousands of protein and antibodies. See page 83 2nd column – last paragraph.

Theses arrays can screen thousands of proteins and are highly economical because they use small amounts of the specimens and reagents. See page 89 2nd column. Arrays are versatile in the biomedical research and clinical medicine. See page 90 1st column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a collection of antibody compositions (1000 different antibodies) to bind a set of 1000 antigens as taught by Cahill in the microarrays of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) because Cahill taught antibody arrays are useful in the detection of proteins, the level of expression of proteins, and the correlation of protein expression in normal versus tumor (disease) tissue. See page 81 2nd column.

Antibody arrays provide high throughput approaches, which allow for the generation and arraying of thousands of protein and antibodies. See page 83 2nd column – last paragraph. Theses arrays can screen thousands of proteins and are highly economical because they use small amounts of the specimens and reagents. See page 89 2nd column.

Response to Arguments

Applicant argues that Cahill is not available as prior art, as claim 79 is supported by the application as filed. However support for claim 79 was not found. The rejection is appropriate.

VI. Claims 31-33, 36, 51-52, 54, 60-61, 74-75, and 81-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879).

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) is set forth above. Specifically, Shalon et al. disclose antibodies immobilized on microarrays while Schuh et al. teach the utility of wherein the antigen specificity is unknown with labeled cell lysates.

Schuh et al. also disclose the use of multiple solid surfaces coated with a plurality of antibodies. These surfaces include microtiter plates, beads, and nitrocellulose membranes. For example, see pages 61-62. However, the references fail to teach the reagents as a kit.
Kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, and instructions are taught. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay microarray and reagents as taught by Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay.

Response to Arguments

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

While a deficiency in a reference may be overcome a rejection under 35 USC 103, a reference is not overcome by pointing out that a reference lacks a teaching for a which other references are relied. *In re Lyons*, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966).

Evidence of commercial success is not persuasive of patentability when the claimed invention would flow logically from the teaching of the prior art. In re Crockett et al. (CCPA 1960) 279 F2d 274, 125 USPQ 186.

VII. Claims 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) as applied to claims 31-33, 36, 51-52, 54, 60-61, 74-75, and 81-83 above, and further in view of Ragg and Whitlow (FASEB, Vol.9, January 1995, pages 73-80).

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) is set forth above.

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) differ from the instant invention in not teaching antibody fragments such as single chain/stranded recombinant antibody compositions.

However, Raag and Whitlow disclose single chain recombinant antibody fragments (sFv) consisting of only the variable light chain (VL) and variable heavy chain (VH) domains covalently linked by a polypeptide linker.

Because the single chain recombinant antibody fragments are small they have rapid pharmacokinetics and tumor penetration in vivo. See abstract. These single chain recombinant antibody fragments are derived from the antigen-binding domain of antibodies and are useful in any molecular recognition or binding application. See page 74 2nd column 2nd paragraph.

SFv's are disclosed as tine reducers in ELISA applications. See page 74 2nd column middle of the 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibody fragments like recombinant single chain/stranded antibodies (sFv) as taught by Raag and Whitlow in the microarray of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) to produce arrays to perform multiple sample analysis in the rapid detection systems because Raag and Whitlow taught that sFv's were small allowing for rapid penetration (abstract), useful in any antibody application (page 74 2nd column 2nd paragraph), and reduced time in ELISA procedures page 74 2nd column middle of the 3rd paragraph.

Response to Arguments

Applicant argues that Raag and Whitlow does not make up for the deficiencies of Shalon et al., Schuh et al., and Foster et al. This argument was carefully considered but not found persuasive because the combination of Shalon and Schuh has been addressed a priori and was maintained. Accordingly the instant rejection is maintained.

VIII. Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) as applied to claims 31-33, 36, 51-52, 54, 60-61, 74-75, and 81-83 above, and further in view of Kohler et al. (Nature, 256, August 7, 1975, pages 495-497).

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) is set forth above.

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) differ from the instant invention in not teaching that the source of the antibodies is from a known hybridoma cell line.

However, Kohler et al. teach antibody production from a known hybridoma cell (tissue culture cell lines made from fused myeloma and spleen cells from an immunized donor). Kohler et al. disclose that the production of antibodies via hybridoma is a satisfactory source of monoclonal antibodies of predefined specificity.

The cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph. The specification teaches that the reference of Kohler et al. teaches hybridoma procedures on page 8 lines 13-19.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize hybridoma cells to produce antibodies as taught by Kohler et al. in the antibody microarray of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) because Kohler et al. taught that hybridoma cells are versatile allowing for antibody production from different origins, can be grown in massive quantity, provide specific antibodies, and could prove valuable for medical and industrial utility. Page 495 1st paragraph and page 497 2nd column last paragraph.

Response to Arguments

Applicant argues that Kohler does not make up for the deficiencies of Shalon et al., Schuh et al., and Foster. This argument was carefully considered but not found persuasive because the combination of Shalon and Schuh has been addressed a priori and was maintained. Accordingly the instant rejection is maintained.

With respect to claim 76, it is noted that priority to 2/4/98 has not been granted because support for the claim has not been exemplified in the originally filed application. Accordingly the claim has been given a priority date of 5/17/06 (the date the claims were filed) for prior art rejections. Applicant is invited to show support for claim 76.

IX. Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) as applied to claims 31-33, 36, 51-52, 54, 60-61, 74-75, and 81-83 above, and further in view of Dolores J. Cahill (Journal of Immunological Methods, 250, 2001m pages 81-91).

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) is set forth above.

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) differ from the instant invention in not teaching the utility of a plurality/collection of 1000 different antibodies.

However, Cahill teach protein and antibody arrays and their utility in medical applications. See abstract. Antibody arrays are disclosed to be useful in the detection of proteins, the level of expression of proteins, and the correlation of protein expression in normal versus tumor (disease) tissue. See page 81 2nd column. Antibody arrays provide high throughput approaches, which allow for the generation and arraying of thousands of protein and antibodies. See page 83 2nd column – last paragraph.

Theses arrays can screen thousands of proteins and are highly economical because they use small amounts of the specimens and reagents. See page 89 2nd column. Arrays are versatile in the biomedical research and clinical medicine. See page 90 1st column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a collection of antibody compositions (1000 different antibodies) to bind a set of 1000 antigens as taught by Cahill in the microarray kits of Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Foster et al. (U.S.Patent#4,444,879) because Cahill taught antibody arrays are useful in the detection of proteins, the level of expression of proteins, and the correlation of protein expression in normal versus tumor (disease) tissue. See page 81 2nd column. Antibody arrays provide high throughput approaches, which allow for the generation and arraying of thousands of protein and antibodies. See page 83 2nd column – last paragraph.

Theses arrays can screen thousands of proteins and are highly economical because they use small amounts of the specimens and reagents. See page 89 2nd column.

Response to Arguments

Applicant argues that Cahill is not available as prior art, as claim 76 is supported by the application as filed. However support for claim 76 was not found. The rejection is appropriate.

X. Claims 66, 67, 68, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) and further in view of Brott et al. (Proceedings of the National Academy of Science, USA, Vol.88, pages 755-759, February 1991).

Shalon et al. (WO 95/35505) in view of Schuh et al. (Journal of Immunological Methods, Vol.152, No.1, 1992, pages 59-67) is set forth above. Shalon et al. in view of Schuh differ from the instant invention in not specifically teaching cell lysate antigens.

However, Brott et al. disclose the evaluation of protein binding patterns (molecular interactions) in cell lysates of GTPase-activating protein (GAP) and two Src Kinases. The researches found that GAP may have a role din mediating normal functions of $p60^{c\text{-}src}$ as well as oncongenic activities of $p60^{v\text{-}src}$. See abstract.

In particular, two different cell lines (cell populations) were employed. The SR-3Yi and NY5H were lysed and the cell lysates incubated with an appropriate antibody. See page 755 2nd - Materials and Methods and page 756 1st column – Antibodies. The protein binding patterns were compared and the differential expression of GAP was analyzed. See figures 1, 2, 3, and 4.

The data presented suggests that normal p60c-src and oncogenic p60v-src are associated with complexes containing GAP in cell lysates. This interaction may contribute to subversion of normal growth control mechanisms. See page 758 2bd column 1st paragraph and last paragraph.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to detect cell lysate analyses as taught by Brott et al. in the microarrays of Shalon et al. in view of Schuh et al. because Brott et al. taught that the data presented suggests that normal p60c-src and oncogenic p60v-src are associated with complexes containing GAP in cell lysates. This interaction may contribute to subversion of normal growth control mechanisms. See page 758 2bd column 1st paragraph and last paragraph.

Response to Arguments

Applicants contend that the combination of references did not teach 1st and 2nd cell lysate measurements. Accordingly the reference of Brott et al. has been added to address the argument.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lisa V. Cook
Remsen 3C-59
(571) 272-0816
6/4/07

LONG V. LE 6/4/07
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600